In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS
No. 21-126V

* *	Chief Special Master Corcoran
TIMOTHY YANNACONE, *	
*	
Petitioner, *	Filed: February 22, 2024
*	
v. *	
*	
SECRETARY OF HEALTH AND *	
HUMAN SERVICES, *	
*	
Respondent. *	
*	
* *	

Ronald Craig Homer, Conway Homer, P.C., Boston, MA, for Petitioner.

Jennifer A. Shah, U.S. Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On January 6, 2021, Timothy Yannacone filed a petition seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program").[2] Petitioner alleges that he incurred a primary cutaneous leiomyosarcoma after receipt of an influenza ("flu") vaccine on September 13, 2018. Petition (ECF No. 1) at 1.

Although the matter had been set for hearing, the parties later agreed that it could be resolved based upon the written filed record (*see* Docket Entry, dated October 5, 2023), including expert reports offered by both sides, and they also opted to rely on their prehearing briefs for their respective positions. *See* Petitioner's Prehearing Submission, dated August 22, 2023 (ECF No. 58) ("Mot."); Respondent's Prehearing Brief, dated September 22, 2023 (ECF No. 59) ("Opp.");

[1] Under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Decision will be available to the public in its present form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) ("Vaccine Act" or "the Act"). Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

Petitioner's Reply, dated October 23, 2023 (ECF No. 61) ("Reply"). Now, for the reasons set forth below, I deny entitlement.

I. Factual Background

Mr. Yannacone (65 years old at the time of the subject vaccination) had a medical history featuring coronary artery disease, high blood pressure, high cholesterol, asthma, chronic obstructive pulmonary disease, and obesity. Ex. 2 at 2, 4. He also had been a smoker (although he had quit almost 20 years before the relevant vaccination). Ex. 3 at 16. In addition, Petitioner had a family history of malignant melanomas, and himself had experienced a number of cancerous skin lesions requiring removal (including a squamous cell carcinoma in 2006, and a basal cell carcinoma ("BCC") on his nose in 2010). Ex. 2 at 4, 282; Ex. 3 at 18.

Petitioner received the "fluzone," high-dose flu vaccine formulation on September 13, 2018, in his left arm. Ex. 21 at 2. Less than one week later, on September 18, 2018, he took himself to urgent care for treatment of knee pain only—but did not at this time complain of any pain or symptoms associated with the prior vaccination. Ex. 11 at 15. Then, on September 28, 2018, he saw his primary care physician ("PCP"), Lance Castellana, M.D., for a wellness exam—again reporting no left arm pain or other issues that might at least temporally have begun close-in-time to vaccination. Ex. 2 at 282. And there is no evidence from this time of any unusual growth or remaining, potentially vaccine-associated skin irritation.

The following month, however (October 9, 2018), after a phone call with Dr. Castellana regarding an unrelated treatment issue, Petitioner for the first time reported some lingering arm soreness associated with where the flu vaccine had been administered to him in September. Ex. 2 at 429. In particular, he stated that it appeared there was "a little pustule in the area" of vaccination, although it did not appear the arm was infected. *Id.* Dr. Castellana advised him to wash and disinfect the area, and to watch for any worsening of symptoms. *Id.*

The next treatment visit relevant to this claim[3] occurred on February 1, 2019—now more than four months post-vaccination. Ex. 2 at 27. Petitioner saw Dr. Castellana at this time, who observed a 5mm nodular lesion on petitioner's left upper lateral arm (in the general area the vaccination had been administered) that was tender to the touch. *Id*. at 29. Dr. Castellana referred Petitioner to a dermatologist, and approximately two weeks thereafter (February 14, 2019) he saw Dr. A. Neal Gregory. Ex. 3 at 3, 14. Petitioner complained of a "painful, tender" small, "pimple-like" bump that he now reported observing after the vaccination. *Id*. at 3.

[3] This record references several intervening medical appointments between October 2018 and February 2019, but it does not appear Petitioner ever complained of any arm-associated issues at these visits. *See generally* Ex. 2 at 27–28.

Dr. Gregory's exam revealed a tender, pink 3-4mm papule on Petitioner's left deltoid, and he deemed it suspicious enough for a biopsy (to potentially rule out a keloid (a raised scar) or other potential issues). Ex. 3 at 3. The biopsy (performed that same month) deemed the lesion to be a "benign palisaded encapsulated neuroma," and Petitioner was diagnosed to have an atypical intradermal smooth muscle neoplasm (i.e., leiomyosarcoma). Ex. 2 at 37; Ex. 3 at 20–21. The pathology report also noted that although excision was recommended, "these tumors rarely ever metastasize" when found in the dermis, as here. Ex. 3 at 21.

On March 23, 2019, Petitioner went back to Dr. Gregory for a surgical excision of the leiomyosarcoma and a further biopsy, which now revealed the existence of residual neoplasm. Ex. 2 at 295; Ex. 3 at 5. On April 22, 2019, Dr. Gregory performed surgery to completely resect the tumor and ensure all cancerous tissue was removed. Ex. 2 at 83. At that appointment, Dr. Gregory commented that the Petitioner had reported he had an "outdoor lifestyle (fishes)" but wore no sunscreen, leading Dr. Gregory to recommend its use in the future. Ex. 3 at 7.

Petitioner's next relevant treatment event occurred in September 2019, when he saw oncologist Peter Lamparello, M.D. Petitioner reported at this time that the soreness he had experienced post-vaccination had lingered. Ex. 4 at 15. An exam of the site of surgery, however, was well-healed. *Id*. at 16. Dr. Lamparello expressed the view that the tumor Petitioner had experience was unlikely to result in spreading cancer, and in fact a CT scan performed that month found no evidence of metastatic disease. *Id*. at 5–6, 17.

Mr. Yannacone returned to Dr. Castellana at the end of 2019 for a wellness exam. Ex. 2 at 409. At this time he expressed concerns about the flu vaccine's role in causing his leiomyosarcoma, noting he had discussed with Dr. Lamparello about whether to receive the vaccine in the future (although Dr. Lamparello did not express an opinion on the topic). *Id.* at 409, 414. E An exam revealed that the scar from Petitioner's excision surgery had healed, even though Petitioner did report it was painful to sleep on. *Id.* at 411. An X-ray performed not long after, however, to assess the presence of potential osteoarthritis produced normal results. *Id*. at 402.

From the winter of 2020 onward, Petitioner continued to complain of some pain at the site of his surgery, as well as more generalized limb or shoulder pain. *See,* e.g., Ex. 3 at 11 (January 2020 visit with Dr. Gregory); Ex. 17 at 3 (January 2021 visit to Dr. Lamparello). But his treaters observed no evidence of tumor recurrence, and instead proposed he seek orthopedic evaluation, to assess if his pain was reflective of some arthritis or tendinitis. Ex. 17 at 6. Petitioner did later obtain orthopedic assistance, first in March 2021, and although initially his symptoms were attributed to impingement or carpal tunnel syndrome, they were effectively treated, at least for a time (with some recurrence in late 2022)—and no vaccine attribution was proposed. *See,* e.g., Ex. 22 at 27–29; Ex. 79 at 6, 8, 10, 13, 14; Ex. 84 at 287; Ex. 79 at 17–18, 30. His cancer has also not recurred.

II. Expert Reports

A. *Kyle Amber, M.D.*

Dr. Amber—a dermatologist with demonstrated expertise in cutaneous immunology—is Petitioner's sole expert, and he prepared two written reports in support of the claim. *See* Report, dated January 26, 2022, filed as Ex. 23 (ECF No. 29-1) ("First Amber Rep."); Report, dated November 17, 2022, filed as Ex. 69 (ECF No. 52-1) ("Second Amber Rep.").

Dr. Amber earned his medical degree from the University of Miami Miller School of Medicine, and completed his Dermatology residency at the University of California Irvine. First Amber Rep. at 1. He is a physician scientist at Rush University Medical Center, specializing in complex medical dermatology, oncodermatology, and general dermatology. *Id*. In his lab, he researches autoimmune skin disease and related cancers. Id. Dr. Amber has written over 100 peer-reviewed publications, and serves as a peer reviewer for major dermatology research journals. *Id*. He is licensed in the state of Illinois, and previously held a medical license in California. *Id*. He has treated two patients with cutaneous leiomyosarcoma (the rare cancer Petitioner had) in the past five years. *Id*.

First Report

Dr. Amber began with a review of the materials he considered in reaching his opinion, followed by an overview of Mr. Yannacone's medical history. *See generally* First Amber Rep. at 2–5. That history, he stated, established that Petitioner had experienced an "atypical smooth muscle neoplasm"—and although Dr. Amber felt it acceptable to refer to it as well as a leiomyosarcoma, he considered Petitioner's actual case to constitute a leiomyosarcoma *variant* with "more indolent features." *Id.* at 6, 11–12. He noted that the pustule that Petitioner had first observed in the post-vaccination period was "curious," however, and could have been something other than tumor (such as folliculitis[4] or a localized reaction to the vaccine's injection). *Id.* at 9. Indeed, even though "[t]he presentation of cutaneous leiomyosarcoma is quite broad," Dr. Amber acknowledged that the record did not sufficiently permit him to evaluate the extent to which symptoms associated with it were also reflective of the later-diagnosed tumor. *Id.* In the end, he deemed the pustule most likely a by-product of the vaccine's administration—but added that secondary impacts from it ("such as a bacterial folliculitis") could still have resulted in the cancer from a "pro-inflammatory cascade." *Id*. at 10.

[4] Folliculitis is "inflammation of a follicle or follicles, usually referring to hair follicles, but sometimes to follicles of other kinds." *Folliculitis*, Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=18992&searchterm=folliculitis (last visited on February 13, 2024)

Leiomyosarcomas generally are benign tumors of the smooth muscles, and can appear on the skin because of hair follicles or other structures where some smooth muscles are present (even though that muscle type does not predominate in the limbs). First Amber Rep. at 6. They are uncommon, and those that occur dermally are unlikely to become metastatic, but can nevertheless be "locally aggressive." *Id.* at 6; *see also* 8. They manifest over long periods of time (months to years), and present as a "cutaneous nodule or mass," usually on the trunk or extremities. *Id.* at 6–7. They are more common in men over the age of 60, and are associated with family melanoma histories. *Id.* at 7, 8, and 9. Dr. Amber also discussed in detail the kinds of protein mutations associated with different forms of leiomyosarcoma and comparable sarcomas, deeming them additional risk factors. *Id.* at 8, 10–11.

Dr. Amber reviewed possible causes of sarcomas, noting that trauma as an instigating factor was "an area of some controversy." First Amber Rep. at 7. Some articles had proposed that prior radiation or trauma could make a person susceptible to a leiomyosarcoma, but he noted that the evidence for this was anecdotal. *Id.;* D. Cook et al., *Atypical Pilar Leiomyomatosis: An Unusual Presentation of Multiple Atypical Cutaneous Leiomyomas*, 40 Journal of Cutaneous Pathology 564, 565 (2013), filed as Ex. 43 (ECF No. 30-1); C. Porter & J. Januszkiewicz, *Cutaneous Leiomyosarcoma,* 109 Plast. Reconstr. Surg. 964, 966 (2002), filed as Ex. 45 (ECF No. 31-3). Some case reports observed leiomyosarcomas arising where tattoo pigments had been inserted into the skin, and another reported one at an insulin injection site (although the latter was more extensive than what Mr. Yannacone experienced). C. West et al., *Cutaneous Leiomyosarcoma Arising in a Tattoo- 'A Tumor With No Humor', 62 Journal of Plastic, Reconstructive & Aesthetic Surgery* e79, e80 (2009), filed as Ex. 47 (ECF No. 31-5)("West"); K. Lunderberg et al., *Invaluable Role of Histopathology in the Diagnosis of Cutaneous Leiomyosarcoma in Insulin Injection Site Reaction*, 14 BMJ Case Reports 1, 5 (2021), filed as Ex. 48 (ECF No. 31-6) ("Lundberg").

Dr. Amber deemed it likely that "trauma of the injection site" was the cause of Petitioner's injury. First Amber Rep. at 6. Mr. Yannacone's likely predisposition (whether as reflected in his family history or some other genetic cause) for sarcoma was thereafter potentially "exacerbated by local hypersensitivity or inflammatory reactions" stemming from the vaccine's administration. *Id.* at 11. To support this causal mechanism, Dr. Amber referenced studies establishing that certain cytokines (some of which help regulate the immune process) reach higher levels in individuals who experience flu vaccine-related reactions or pain. L. Christian et al., *Proinflammatory Cytokine Reponses Correspond With Subjective Side Effects After Influenza Virus Vaccination*, 33 Vaccine 3360, 3366 (2015) filed as Ex. 64 (ECF No. 43-15) ("Christian"). These cytokines, Dr. Amber proposed, were "plausible contributors" to activation of an enzymatic pathway responsible for cell proliferation (and hence associated with cancer) that likely could encourage the development of a leiomyosarcoma. First Amber Rep. at 11; J. Cui et al., *Macrophage Migration Inhibitory Factor Promotes Cardiac Stem Cell Proliferation and Endothelial Differentiation Through the Activation*

of the PI3K/Akt/mTOR and AMPK Pathways, 37 International Journal of Molecular Medicine 1299, 1309 (2016), filed as Ex. 63 (ECF No. 33-1); O. Ozes et al., *A Phosphatidylinositol 3-kinase/Akt/mTOR Pathway Mediates and PTEN Antagonizes Tumor Necrosis Factor Inhibition of Insulin Signaling Through Insulin Receptor Substrate-1*, 98 Proceedings of the National Academy of Sciences of the United States of America 4640, 4645 (2001), filed as Ex. 65 (ECF No. 33-3).

Dr. Amber admitted, however, that he could point to no studies involving smooth muscle cells in which such immune-mediated cytokine activation resulting in tumor/cancer activation had been evaluated or observed. First Amber Rep. at 11. He similarly noted he had identified few studies showing that the flu vaccine specifically could trigger a leiomyosarcoma. *Id.* at 12. At most, one case report observed a leiomyosarcoma developing at the situs of administration for a *smallpox* vaccine, and long after as well. M. Patel et al., *Cutaneous Desmoplastic Leiomyosarcoma Development at Smallpox Vaccination Site*, 19 Skinmed 462, 463 (2021), filed as Ex. 67 (ECF NO. 33-5) ("Patel") (case study of an 81-year-old man diagnosed with desmoplastic leiomyosarcoma at the site of a past smallpox injection, which enlarged over a period of four years). And he referenced again Lundberg, which involved an association between the situs of an insulin injection site and cutaneous leiomyosarcoma, albeit with a clinical course exacerbated by other health issues. But he disputed there were other explanations for the leiomyosarcoma, such as a pre-vaccination, sub-clinical sarcoma (which the record did not support), or simply some idiopathic occurrence. First Amber Rep. at 12.

The timeframe from vaccination to Petitioner's development of leiomyosarcoma was also deemed medically acceptable by Dr. Amber, and the medical records showed the cancerous process unfolding in a manner consistent with his causation theory. First Amber Rep. at 11. The pustule and associated pain that Petitioner complained of a month after vaccination occurred in the time period consistent with post-vaccination cytokine elevation. S. Mohanty et al., *Prolonged Inflammatory Cytokine Production in Monocytes Modulated by Interleukin 10 After Influenza Vaccination in Older Adults*, 211 Journal of Infectious Disease 1174, 1184 (2015), filed as Exhibit 66 (ECF No. 33-4) ("Mohanty"). The secondary activation of the enzymatic pathway that would lead to tumor/sarcoma development would occur more quickly, and thus its later diagnosis timeframe was acceptable (although Dr. Amber again deemed it "unclear" whether the pustule *itself* was a manifestation of the leiomyosarcoma or instead "an intermediate step" between vaccine administration and tumor development). First Amber Rep. at 11.

Second Report

Dr. Amber offered a final written report reacting to criticisms lodged by Respondent's experts (Drs. Hedrick and Maverakis). At the outset, he emphasized his view that the fact that the leiomyosarcoma just happened to appear post-vaccination but "in the same anatomical vicinity" as the vaccination was unlikely the product of mere chance—especially since there existed a

compelling "biochemical rationale" to explain how one could lead to the other. Second Amber Rep. at 2, 4. He admitted, however, that the vaccine was not likely the only explanatory factor (and if it were, post-vaccination leiomyosarcomas would be more commonly seen), but instead was probably only one causal element (along with Petitioner's other risk factors). *Id.* Otherwise, the fact that the etiology of leiomyosarcomas was not fully understood was likely attributable to the difficulty in studying "such a rare and poorly defined tumor." *Id.*

Next, Dr. Amber responded to the argument of Respondent's experts that the location of Petitioner's injury was itself a basis to doubt causation, since vaccines are administered into skeletal muscles, whereas a dermal leiomyosarcoma only affects smooth muscles. Second Amber Rep. at 2. He agreed there would be no "direct association" between smooth muscles in the arm (which would be found there only in connection with hair follicles) and skeletal muscles, but proposed that "the arrector pili's involvement"[5] was still possible. Even if the total distribution of these smooth muscles in the arm was limited, that only meant to Dr. Amber that the risk of "damage to many arrector pili remains low"—not that a single one could not plausibly have been "hit." *Id.* (emphasis in original). And even if it were true (as Dr. Amber conceded) that leiomyosarcomas were not generally understood to be caused by direct muscle trauma, his analysis did not rely on this explanation for Petitioner's injury (although he did not explain how this concession impacted his parallel argument that needle trauma to an arrector pili muscle had triggered the leiomyosarcoma in this instance). *Id.* at 3.

Dr. Amber more strenuously contended that the borderline character of a cutaneous leiomyosarcoma—as something that was "not quite cancer, but . . . doesn't quite fit well with hyperplasia or dysplasia alone"—meant that common thinking about the nature of (and timeframe for) carcinogenic pathology was not useful in understanding what Petitioner had experienced. Second Amber Rep. at 3–4. While Dr. Amber agreed that "acute immune reactions do not result in acute tumor formation," a person with a number of concurrent predisposing factors could still develop a tumor akin to what Petitioner experienced, with the immune reaction associated with vaccination acting as the "final insult." *Id.* (emphasis in original).

This would occur, he emphasized, through the vaccine's well-understood capacity for stimulation of "[a]cute inflammatory cytokines." Second Amber Rep. at 4. Certain cytokines were known to impact and affect dysplasia and hyperplasia. J. Youn et al., *Regulation of TNF-a-mediated Hyperplasia Through TNF Receptors, TRAFs, and NF-kB in Synoviocytes Obtained From Patients With Rheumatoid Arthritis*, 83 Immunology Letters 85, filed as Ex. 72 (ECF No. 52-4); J. Chadwick et al., *TNFα Signaling Is Increased in Progressing Oral Potentially Malignant Disorders and Regulates Malignant Transformation in an Oral Carcinogenesis Model*, 11 Frontiers in Oncology 1, 14 (2021), filed as Ex. 74 (ECF No. 52-6). This capacity was likely greater

[5] Dr. Maverakis's report defines arrector pilli as "the very small muscles in the skin dermis that are attached to hair follicles." Maverakis Rep. at 8.

"in already partially diseased tissue," which Dr. Amber seemed to believe would be prevalent in an individual "with a predisposition towards developing cancer." Second Amber Rep. at 4. And this was possible even if the vaccine-caused upregulation of pro-inflammatory cytokines was transient. What mattered, he contended, was the vaccine-induced increase of these cytokines—which would occur in tissue as well as blood serum, and could stimulate different inflammatory pathways associated with tumorigenesis (even if his initial focus on a different enzymatic pathway was incorrect).

Regarding the flu vaccine specifically, Dr. Amber did not deem significant the fact that Petitioner's treaters had not directly or indirectly proposed a causal relationship. In his experience most treaters would inherently emphasize the benefits of vaccination—and therefore Dr. Lamparello's seemingly-ambivalence about the need for Petitioner to receive the flu vaccine in the future "indicates some level of concern regarding the association" (even though the record at issue plainly indicates Dr. Lamparello simply opted not to entertain the question of vaccine causation—*not* that he deemed it a difficult issue to opine upon). Second Amber Rep. at 2–3; Ex. 2 at 410 ("Please note: he discussed having a flu vaccine with Dr. Lamparello of Hematology/Oncology. He notes that Dr. Lamparello did not advise him one way or the other- per patient.").

Finally, Dr. Amber reiterated his view that the Petitioner possessed several risk factors that the vaccination likely amplified. For example, although he agreed with Respondent's experts that there was a low risk Petitioner suffered from "a familial melanoma syndrome," he nevertheless opined that certain genetic mutations were relevant to a predisposition to melanoma, and which could be relevant herein. Second Amber Rep. at 3. The same was true of a likely tendency toward immunosuppression in individuals with leiomyosarcomas. *Id.*

B. *Emanual Maverakis, M.D.*

Dr. Maverakis is a dermatologist and immunologist, and he offered a reaction on Respondent's behalf to Dr. Amber's causation theory. *See* Report, dated June 26, 2022, filed as Ex. A (ECF No. 42-1) ("Maverakis Rep.").

Dr. Maverakis earned his medical degree from Harvard Medical School. Maverakis Rep. at 1. He then completed an internship in internal medicine at the Beth Israel Deaconess Medical Center, and dermatology residency at the University of California, Davis. *Id*. He has published 185 peer-reviewed manuscripts, and has received various research awards throughout his career. *Id*. He is currently a tenured professor at the University of California, Davis, and serves as the Director of Autoimmunity and the Director of Immune Monitoring. *Id*. In his clinical practice, he specializes in treating patients with rare skin cancers and rare immune-mediated diseases. *Id*. at 2.

The initial section of Dr. Maverakis's Report outlined the materials he reviewed in preparation of his opinion, and summarized Petitioner's medical history. *See generally* Maverakis Rep. at 2–7. He then turned to a discussion of Petitioner's injury. He characterized leiomyosarcoma to be an "extremely rare tumor," reflecting two to three percent of all soft tissue sarcomas. *Id.* at 8; J. Kohlmeyer et al., *Cutaneous Sarcomas*, 15 Journal of the German Society of Dermatlogy 630, 639 (2017), filed as Ex. A, Tab 1 (ECF No. 43-1). The type experienced by Petitioner, a dermal leiomyosarcoma, was least likely to metastasize, and Dr. Maverakis agreed with Respondent's other expert, Dr. Hedrick, that because of this the diagnostic term "sarcoma" was arguably incorrect (noting leiomyosarcoma might be more precisely understood to be an "atypical intradermal smooth muscle neoplasm"). Maverakis Rep. at 8. Their situs distribution on the skin was variable, and their cause was deemed largely to be idiopathic, with no fully-understood triggers. *Id;* B. Llombart et al., *Leiomyosarcoma and Pleomorphic Dermal Sarcoma: Guidelines for Diagnosis and Treatment*, 110 Actas Dermosifiliogr (Engl. Ed) 4, 11 (2019), field as Ex. A, Tab 5 (ECF No. 43-5).

Dr. Maverakis also explained that a leiomyosarcoma occurs only with smooth muscle tissue—one of three muscle types (the others being skeletal and cardiac), but *not* the kind of muscle tissue predominating in the deltoid, where vaccines are administered. Maverakis Rep. at 7, 8. Indeed, Dr. Maverakis deemed it almost "inconceivable that a vaccine administered to skeletal muscle can cause a tumor of smooth muscle origin." *Id.* at 8. Dr. Maverakis acknowledged that a "very small" smooth muscle cell found in the skin dermis of the arm (such as those in hair follicles) could be the locus of the form of leiomyosarcoma Petitioner experienced—although for vaccine causation to hold, the follicle would have to have been "damaged as the needle used to administer the influenza vaccine passed through," and Dr. Maverakis deemed this "highly unlikely" to have occurred—for several reasons. *Id.*

First, Dr. Maverakis contended, injury to the "extremely small" arrector pili muscle in the hair follicle occurring incidental to vaccine administration was itself improbable (independent of whether a leiomyosarcoma would then develop). The follicles in question to which these smooth muscles are attached are not only miniscule in diameter (although not much larger than a needle) but are also highly limited in distribution of the skin—reducing the possibility a needle would inadvertently encounter that specific muscle. Maverakis Rep. at 9 ("a needle passing through the skin above the deltoid region is not likely to encounter many, if any, arrector pili muscles").

In fact, trauma of *any* kind as a precursor for leiomyosarcoma was unlikely, as reflected in the literature. Maverakis Rep. at 9; C. Queiros et al., *Cutaneous Leiomyosarcoma: A 20-Year Retrospective Study and Review of the Literature*, 96 Anais Brasileiros de Dermatologia 278, 280, filed as Ex. 39 (ECF No. 30-7) ("[h]owever, most cutaneous LMS originate again, with no prior triggering factor"). And Petitioner's case reports were not strongly supportive of trauma as instigative of a leiomyosarcoma. One case report, for example, referred to a "foreign body" in the

skin as a supposed trigger, and yet (a) the clinical findings reported in the article did not reflect proof of it, and (b) the alleged trauma predated the tumor *by months* (not almost contemporaneously, as here). F. Cammisuli et al., *A Painful Nodule on the Leg: A Quiz*, 95 Acta Derm. Venereol 633, 635 (2015), filed as Exhibit A, Tab 9 (ECF No. 43-9). This was even more so in West, where the tattoo identified as causal had been created *ten years* before the cancer's development (consistent with what is known about cancer's time course, but not with the facts of this case). West at e79.[6] And the Lundberg case report involved an individual who had *for years* been injecting insulin into the same site as where a leiomyosarcoma developed—with insulin itself (unlike the flu vaccine's components) deemed a "growth factor for cancer cells." Maverakis Rep. at 10; Lundberg at 1; H. Yamamoto et al., *Insulin-Like Growth Factor II Messenger RNA–Binding Protein 3 Expression in Gastrointestinal Mesenchymal Tumors*, 45 Human Pathology 481, 487 (2014), filed as Ex. A, Tab 12 (ECF No. 43-12).[7]

Second, Dr. Maverakis expressed doubt that the inflammatory response to vaccination was robust enough to cause "the malignant transformation" of the hair follicle's smooth muscles. Maverakis Rep. at 9. Any localized, inflammatory vaccine reaction would usually be evidenced by a transient occurrence of redness and swelling—yet Petitioner never reported any such response. *Id.* And a short-lived, immune-mediated inflammatory response (reflecting cytokine upregulation) consistent with what vaccines are known to spark would not itself likely result in a cancerous process consistent with the timeframe Petitioner experienced (at most, four to five months from vaccination to the time the growth was large enough to be identified as a tumor). This timeframe was not consistent with the longer temporal horizon for the development of cancer. *Id.* at 9–10; D. Malkin et al., *Germ Line p53 Mutations in a Familial Syndrome of Breast Cancer, Sarcomas, and other Neoplasms*, 250 Science 1233, 1238 (1990), filed as Ex. A, Tab 7 (ECF No. 43-7).

Relatedly, Dr. Maverakis did not deem persuasive the contention that the flu vaccine could mechanistically cause a leiomyosarcoma through cytokine-induced stimulation of certain enzymatic pathways involved in cell growth. Maverakis Rep. at 11–12. Even if the general concept that vaccination caused upregulation of cytokines was scientifically reliable, those increases were "transient and extremely short-lived." *Id.* at 12; Christian at 11, Figure 1 (levels of TNF and MIF returning to baseline within 4 days). Post- vaccination cytokine elevations (in comparison to a pre-

[6] In addition, Dr. Maverakis emphasized, tattooing involves the use of larger, ink-bearing needles that repeatedly puncture the skin, at a rate of hundreds or thousands of times per minute—far more trauma than what occurs in connection with a one-time vaccination. Maverakis Rep. at 10.

[7] Dr. Maverakis also denied that Patel (a case report involving the smallpox vaccine) corroborated the purported flu vaccine-leiomyosarcoma association, noting that (a) the smallpox vaccine was distinguishable, and discontinued nearly 50 years ago, (b) there was a years-long temporal gap in the Patel case study, from vaccination to the leiomyosarcoma's development in that case, and (c) the smallpox vaccine was *not* administered intramuscularly but literally into the skin itself. Maverakis Rep. at 12–13.

vaccination, baseline level) in fact only lasted for a few days, and were modest in magnitude as well. Maverakis Rep. at 12. And there was a meaningful "distance" (immunologically-speaking) from the deltoid muscles, where the vaccine's antigens would first cause cytokine increases, to the smooth muscle cells on the skin's surface that would constitute the locus for the tumor development, further reducing the likelihood that cytokine increases attributable to vaccination could induce a cancer in the short time generally the cytokine increase would be observed. *Id.*

Other factors identified as possibly contributory by Dr. Amber did not merit weight, in Dr. Maverakis's view. Petitioner's melanoma family history did not mean that he himself had inherited a genetic risk—especially since he was at the age where it should have presented. Maverakis Rep. at 11.[8] And the medical record did not corroborate the presence of some of the mutations associated with heredity melanoma. *Id.* Dr. Amber's speculation that Petitioner's injury could have been in part the by-product of a folliculitis instigated by vaccination was also rejected by Dr. Maverakis, who noted that there was no association between folliculitis and cancer (except for rare chronic folliculitis variants inconsistent with what Petitioner experienced). L. Ding et al., *Giant Cutaneous Squamous Cell Carcinoma of the Scalp Arising in the Setting of Folliculitis Decalvans*, 15 BMJ Case Reports 1, 4 (2022), filed as Ex. A, Tab 14 (ECF No. 43-14).

Finally, Dr. Maverakis stressed some record points that he deemed unsupportive of causation. In particular, he noted that the record established only that *Petitioner* opted against taking the flu vaccine in the future—not that he received such advice from treaters—and hence this did not stand as evidence treaters accepted the flu vaccine as causal. Maverakis Rep. at 9–10.

C. *Dr. Stephen M. Hedrick, Ph.D.*

Dr. Hedrick, a professor of immunology, offered a single written report for Respondent. See Report, filed June 30, 2022, as Ex. C (ECF No. 42-3) ("Hedrick Rep."). He opined that the flu vaccine could not immunologically cause a tumor/leiomyosarcoma.

Dr. Hedrick received his Ph.D. in molecular Biology and biochemistry from UC Irvine, and the completed a postdoctoral fellowship at the National Institutes of Health. Hedrick Rep. at 1. For nearly 40 years, he taught courses on immunology, virology, and the history and biology of epidemic diseases at the University of California, San Diego. *Id*. He also operated a research laboratory studying T cell immunology during this time. Id. He has published more than 200 peer-reviewed articles. *Id*. He served as Chair of Biology, and then Chair of Molecular Biology at UC San Diego for a total of seven years. *Id*. He retired in 2021, and is currently a Distinguished Professor, Emeritus. *Id*.

[8] Of course, the record in this case *does* establish that Petitioner experienced some melanomas pre-vaccination.

After noting the review of records he had performed for his work on the case and providing a short summary of Petitioner's history, Dr. Hedrick offered a brief explanation of leiomyosarcoma. *See generally* Hedrick Rep. at 2–3. Smooth muscles, he noted, often help with blood vessel contraction regulation—but "form the arrector pili of the hair follicle" when found on the skin. *Id.* at 2. The kind of cutaneous leiomyosarcoma Petitioner experienced is uncommon, occurring at the surface skin level, and is "very rarely metastatic"; indeed, Dr. Hedrick seemed to agree with Dr. Amber that it might be better to characterize Petitioner's injury as an atypical smooth muscle neoplasm, since "sarcoma" implied something more progressive. *Id.* at 2, 4*;* S. Kraft & C. Fletcher*, Atypical Intradermal Smooth Muscle Neoplasms: Clinicopathologic Analysis of 84 Cases and a Reappraisal of Cutaneous "Leiomyosarcoma."* 35 American Journal of Surgical Pathology 599, 607 (2011), filed as Ex. 32 (ECF 29-10). They also were more common in late middle-aged men. Hedrick Rep. at 3.

The etiology of leiomyosarcoma is not well understood, Dr. Hedrick maintained—especially since it is often lumped together in studies with soft tissue sarcomas arising elsewhere in the body. Hedrick Rep. at 2. He concurred with Dr. Amber that some might be associated with prior trauma (although he noted that the case reports proposing the association often involved long-resolved scar tissue – not immediately-recent vaccinations) or cancer-instigating viruses. *Id.* at 2, 3. Otherwise, leiomyosarcoma had been associated with immunodeficiencies, whether attributable to an infection or some outside environmental toxin. M. Shiels & E. Engels, *Increased Risk of Histologically-Defined Cancer Subtypes in HIV-Infected Individuals: Clues for Possible Immunosuppression-Related or Infectious Etiology*, 118 Cancer 4869, 4876 (2012), filed as Ex. C, Tab 8 (ECF No. 44-8). It might be that leiomyosarcomas tend to arise in "immune-privileged" locations (like scarred tissue), where "local immune surveillance" that might otherwise inhibit growth of the tumor was absent. J. Bostwick et al*., Marjolin's Ulcer: An Immunologically Privileged Tumor?*, 57 Plastic Reconstructive Surgery 66, 69 (1976), filed as Ex. C, Tab 10 (ECF No. 44-10).[9] Dr. Hedrick also agreed with Dr. Amber that leiomyosarcomas were likely associated with certain genetic "missense" mutations leading to protein encoding errors (even though to some extent this was common to all tumors). Hedrick Rep. at 2–3.[10]

[9] In fact, Dr. Hedrick observed, the very fact a leiomyosarcoma might arise in such an immune-privileged location could also explain its non-metastatic, benign character—since the cancerous cells involved would be immediately recognized and attacked by the immune system upon attempting to "leave" their cutaneous site of origin. Hedrick Rep. at 2; J.D. Bui & R.D. Schreiber, *Cancer Immunosurveillance, Immunoediting and Inflammation: Independent or Interdependent Processes?*, 19 Current Opinion in Immunology 203, 208 (2007), filed as Exhibit C, Tab 11 (ECF No. 44-11).

[10] Dr. Hedrick gave less weight to a family history of melanomas (as is true of Petitioner) as a risk factor, however, noting that Dr. Amber's support for this contention was a 1997 article published by a medical student. C. Berking & M. Brady, *Cutaneous Melanoma in Patients with Sarcoma*, 79 Cancer 843, 848 (1997), filed as Ex. 41 (ECF No. 30-9) ("Berking"). In addition, Berking observed the same percentage of leiomyosarcomas in those patients with distinguishable soft tissue sarcomas (8 out of 41 or 21 percent) as those without melanomas at all – undermining the conclusion that there was any real melanoma association. Hedrick Rep. at 4–5; Berking at 845. Otherwise, the fact

Dr. Hedrick strenuously disputed the existence of a link between leiomyosarcoma and vaccination, noting that his own electronic searches for an association between the two almost wholly produced articles "directed toward using vaccines to treat cancer." Hedrick Rep. at 3. At best, he identified Patel, with the tumor "arising from a scar that was at least 50 years old," and also associated with a different vaccine not widely administered for longer than that period of time. *Id;* Patel at 1. The passive-surveillance "VAERS" system[11] similarly identified few cases of claim connecting the flu vaccine to leiomyosarcoma—and nothing specific to the vaccination situs issue that is relevant to this claim. Hedrick Rep. at 3.

In addition, Dr. Hedrick opined that the immune-mediated mechanism proposed by Dr. Amber was not likely to cause oncogenesis. Hedrick Rep. at 3–4. He attributed cancerous disease processes to "profound dysregulation of the cellular pathways controlling cell growth," along with the failure of "inhibitory feedback controls." *Id.* at 3. These process failures would normally not occur absent aberrant gene activity—making it implausible that tumor formation could occur simply as a result of an immune response. Indeed, vaccination would produce "very mild inflammatory signals" that would involve upregulation of certain cytokines, but that were not likely to encourage tumor growth via the pathways Dr. Amber proposed. *Id.*at 3–4.

Nor, Dr. Hedrick opined, had Dr. Amber bulwarked his theory with adequate independent evidentiary support. Christian, for example, did observe some relationship between serum levels of specific cytokines and vaccination side-effects. Christian at 11–13. But the varied cytokine levels between those who did, or did not, experience more significant soreness occurred in groups that all began healthy, suggesting that cytokine levels alone could not explain why some did, or did not, experience greater side effects post-vaccination. Hedrick Rep. at 4. And the number of subjects, plus other methodologic limits of the Christian study, further reduced its predictive value. Other articles cited by Petitioner, like Mohanty, only showed increased cytokines observed in the studied patients, as opposed to "the accumulation of system" cytokines, which would be more significant to the argument that overall, progressive cytokine increases were causing harm (as

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that Petitioner's family had experienced melanomas was not supported by evidence that Petitioner himself had inherited from them some identifiable genetic risk factor.

[11] "VAERS," or the Vaccine Adverse Event Reporting System, is a passive surveillance system maintained by the Center for Disease Control, in which anyone may file a report alleging that a vaccine caused a particular injury, illness, or death. As discussed by other special masters, the data provided by VAERS does not illustrate a causal connection; rather, VAERS exists to prompt further scientific investigation into potentially dangerous vaccines. *See*, e.g., *Tompkins v. Sec'y of Health & Human Servs.*, No. 10-261V, 2013 WL 3498652, at *9 n.25 (Fed. Cl. Spec. Mstr. June 21, 2013), *mot. for review denied*, 117 Fed. Cl. 713 (2014). VAERS reports are informal and unverified, and should not be confused with formal case reports in medical literature. *Tompkins,* 2013 WL 3498652, at *9 n.26. For these reasons, other special masters have consistently declined to rely on VAERS data as probative with regard to vaccine causation. See, e.g., *Analla v. Sec'y of Health & Human Servs*., 70 Fed. Cl. 552, 558 (2006); *Ryman v. Sec'y of Health & Human Servs.*, 65 Fed. Cl. 35, 39–40 (2005).

opposed to simply increasing transiently). Mohanty at 1176–1180. And Petitioner had been vaccinated before to no ill effect, further undermining cytokine upregulation as explanatory.

Ultimately, Dr. Hedrick maintained that Petitioner's causation theory mostly if not wholly relied on the temporal association between vaccination and appearance of his leiomyosarcoma later, along with the situs coincidence. But this did not provide a "genetic or biochemical basis" to find an association between injury and vaccine. Hedrick Rep. at 5. The lack of established association was, in Dr. Hedrick's view, especially glaring given the huge number of flu vaccine administered each year—yet without reports of a comparable adverse event *or* scientific/medical evaluations of a possible relationship.

III. Procedural History

As noted, this claim was initiated in January 2021. After it was activated out of "pre-assignment review" (meaning sufficient records had been filed for the claim to proceed) in April 2021, it was assigned to a different special master, before reassignment to me that August. Respondent's Rule 4(c) Report contested entitlement, and the parties subsequently filed the above-referenced expert reports. A year later, I set the matter for hearing and a schedule for filing briefs in connection with each party's position. Prehearing Order, dated September 14, 2022 (ECF No. 50). But the parties informed me in October 2023 that they agreed no hearing would be required, and were instead prepared to have the matter resolved on the papers, and based on their prehearing filings as well. Accordingly, the claim is ripe for resolution.

IV. Parties' Arguments

A. *Petitioner*

Petitioner first asserts that his diagnosis of primary cutaneous leiomyosarcoma was correct. He references multiple instances in treater notes where physicians either stated directly that Petitioner had cutaneous leiomyosarcoma, or stated that he had abnormal smooth-muscle neoplasms, which Dr. Amber deemed an alternative name for the condition. Mot. at 16-20.

Then, Petitioner discusses his "can cause" argument. Dr. Amber noted medical literature connecting primary cutaneous leiomyosarcoma development to physical skin trauma. Mot. at 21. Because there are approximately 35 arrector pilli per square centimeter under the skin, the 0.6mm needle used to administer the flu shot could easily cause damage. *Id.* at 22. He also supported this with the Patel case study, showing development of a leiomyosarcoma at the site of administration of a smallpox vaccine. A local reaction, combined with genetic predisposition such as family history, could combine to lead to leiomyosarcoma development. *Id.* at 23. The inflammatory cytokines triggered by flu vaccination have also been shown in certain items of literature to

stimulate pathways of tumorigenesis. *Id.* at 23–27. Further, Dr. Amber explained that it was "highly unlikely" that Petitioner would have developed a leiomyosarcoma in the exact spot where he was vaccinated by coincidence. *Id.* at 23. Given the significant connection between trauma and leiomyosarcoma supported in medical literature, and his multiple risk factors, he has presented sufficient evidence for a medical theory connecting his flu vaccination and leiomyosarcoma. *Id.* at 27.

Regarding the "did cause" prong, Petitioner emphasized again that he had developed primary cutaneous leiomyosarcoma at the exact site where he received the vaccination. Further, multiple studies state that leiomyosarcoma is most commonly found on the head, neck, and lower extremities. Mot. at 28–29. Thus, the unusual location of his leiomyosarcoma also lends itself to a causal link. And neither treating physicians nor respondent identified any potential alternative causes of his leiomyosarcoma (although none connected the two either).

Finally, the initial development of his leiomyosarcoma (beginning with a small pustule at the injection site) aligns with estimates of the rise of pro-inflammatory cytokines established in medical literature—between 1 and 28 days. *See* Amber First Rep. at 11. Petitioner first contacted his primary care physician about the pustule 26 days after vaccination. The pustule worsened over the coming months, eventually resulting in his leiomyosarcoma diagnosis. Thus, he states, he has established a proximate temporal relationship between the vaccine and his leiomyosarcoma.

B. *Respondent*

Respondent contends that the causation theory offered herein is fundamentally "inconceivable" due to the mechanics of the flu vaccine. Opp. at 11. The flu vaccine is administered directly into the skeletal muscle—but leiomyosarcomas develop from smooth arrector pilli muscles, a completely different type of muscle. Thus, a vaccine administered into skeletal muscle could not likely cause a tumor in the smooth muscles. *Id.*

Respondent goes on to argue that Petitioner's two proposed causal theories are speculative. First, he addresses Dr. Amber's theory that direct trauma from the vaccine needle damaged the arrector pilli muscles, causing the leiomyosarcoma to arise. Opp. at 12. Dr. Amber himself admits in his reports that the association between trauma and leiomyosarcoma in the literature is not well-established. *Id.* The studies Dr. Amber cited, moreover, were case reports rather than epidemiological studies or clinical trials. *Id.* at 13. And even the case reports were not analogous to Petitioner's course, since they involved different types of skin traumas, occurring years before the leiomyosarcomas developed. *See,* e.g., Patel, Lundberg, and West.

Respondent also addresses Dr. Amber's second theory: that the local inflammatory response caused by the flu vaccine resulted in malignant transformation of arrector pilli muscle

cells. Opp. at 16. First, he points out that any rise in inflammatory cytokines would be highly transitory, and thus would not align with the typical development of cancers over a period of years, involving profound dysregulation of cellular pathways. Further, the pro-inflammatory cytokines identified by Petitioner are too mild to cause such dysregulation. *Id.* at 17. Finally, the studies Dr. Amber cites, such as Mohanty, examine only a temporary rise in cytokines, and do not address the *systemic* accumulation of these cytokines that would need to occur to support Petitioner's theory. *Id.* at 18. In addition, Respondent contests Dr. Amber's argument that inflammatory cytokines produced by the flu vaccine served as the "last straw" for a patient with numerous leiomyosarcoma risk factors to develop the uncontrolled proliferation of cells, pointing out that he does not provide any scientific literature supporting this theory, nor does he propose a mechanistic explanation. *Id.* at 19.

Otherwise, Respondent contends that Petitioner has failed to establish a logical sequence of cause and effect between his vaccination and development of leiomyosarcoma. He deems Dr. Amber's reliance on the Christian study to support his inflammation hypothesis as misguided, given that the patients in that study had *local* site reactions to vaccines, unlike Petitioner. Opp. at 20. Dr. Amber's argument that appearance of a leiomyosarcoma on the shoulder is uncommon is also incorrect. *Id.* at 21. And Petitioner's treating physicians' inability to find an alternative cause for his sarcoma is unsurprising, as literature shows that most cases of leiomyosarcoma are idiopathic.

Finally, Respondent disputed Petitioner's success in proving a medically acceptable onset timeframe measured from vaccination. According to Dr. Maverkis, cancers develop over a course of *years* rather than weeks, even in extreme cases. Opp. at 21. Further, the studies Dr. Amber cited in his reports to assert that inflammatory cytokines could cause rapid cell proliferation were not performed on humans. *Id.* at 22.

V. Applicable Legal Standards

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed.

Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[12] Petitioner does not herein assert a Table claim, nor does one exist specific to the alleged injury.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health and Hum. Servs.,* 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury."

Each *Althen* prong requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing

[12] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. App'x. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

Capizzano, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245 ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)).

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." (citing *Moberly*, 592 F.3d at 1322)); *see also Howard v. Sec'y of Health & Hum. Servs*., 2023 WL 4117370, at *4 (Fed. Cl. May 18, 2023) ("[t]he standard has been preponderance for nearly four decades"), *appeal docketed,* No. 23-1816 (Fed. Cir. Apr. 28, 2023). And petitioners always have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y*

of Health & Hum. Servs., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral or written testimony (provided in the form of an affidavit or declaration) may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

In the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings, like the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have

been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not all such items factor into the outcome of this decision. While I have reviewed all the medical literature submitted, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, No. 2015–5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

ANALYSIS

Petitioner has not met his burden of proof under *Althen*.[13] First, insufficient evidence has been offered to establish that the flu vaccine can cause a leiomyosarcoma. Dr. Maverakis persuasively established that it is unlikely generally that a vaccine intended to be administered to skeletal muscles would, in the process of administration, "hit" the far less common smooth muscle cells located in hair follicles on the arm. Moreover, insufficient evidence was offered in this case through Dr. Amber to suggest that vaccines have ever been considered to have this sarcoma-causing capacity—and due, moreover, to incidental trauma to a smooth muscle cell. The case reports Petitioner offers are factually distinguishable, as noted above, and in any event are not a kind of evidence given great weight in Program cases. *Crutchfield v. Sec'y of Health & Hum. Servs.*, No. 09-0039V, 2014 WL 1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014), *mot. for review den'd*, 125 Fed. Cl. 251 (2014) ("single case reports of Disease X occurring after Factor Y…do not offer strong evidence that the *temporal* relationship is a causal one—the temporal relationship could be pure random chance").

Otherwise, the argument that the immune stimulation that vaccines generally (and in fact are intended to) provoke could result in a cancerous process relies too much on the *expected* function of a vaccine progressing pathologically, but without supplying the necessary connective proof. This kind of contention is often advanced in Vaccine Act claims—but reasonably rejected. *Palattao v. Sec'y of Health & Hum. Servs.*, No. 13-591V, 2019 WL 989380, at *36 (Fed. Cl. Spec. Mstr. Feb. 4, 2019) ("claimants cannot transmute scientific evidence exploring how vaccines normally function in the immune system into a reliable and persuasive causation theory that any vaccine can be pathogenic without a more specific showing that applies to the circumstances at hand"). And certainly little to nothing has been offered in this case that would evidentially support this cytokine-encouraged mechanism as applicable to development of leiomyosarcoma—even in an individual with a suspected predisposition.

Second, I cannot conclude it preponderantly likely that the flu vaccine Petitioner *did* receive was the reason for the skin tumor he later developed. There is, at the outset, no treater support for a flu vaccine association with Petitioner's injury (although I do not give this alone great weight, since the rarity of the injury at issue would not likely be suspected as vaccine-related). But the record more broadly does not support the conclusion that Petitioner's vaccination had anything to do with the leiomyosarcoma, beyond the general fact that both occurred in approximately the same area of his arm. The pustule that Petitioner seems to identify as what later became the leiomyosarcoma was itself not identified until a month post-vaccination—and thereafter was not again in the record raised as an issue until February 2019, more than four months after the September vaccination. Preponderant evidence does not support the determination that this reflects

[13] Because the first two prongs are not met, I do not discuss Petitioner's prong three showing—since its success would not save the claim.

a steady progression from pustule to leiomyosarcoma (as opposed to a sarcoma-like growth occurring in the same situs coincidentally).[14] The fact that no immediate reaction to the vaccine was reported bulwarks my conclusion (as this is not a case where a claimant identified some kind of post-vaccination skin trauma at the situs and then recorded complaints about its progression). And there is no other record proof suggestive of the vaccine as a trigger—it simply preceded temporally the date by which the leiomyosarcoma appeared.

It is undoubtedly the case that the development of Petitioner's tumor near, or even at, the situs of vaccination in this case raised reasonable causation suspicions. A vaccination *could* result in some kind of localized reaction, perhaps equivalent to the pustule Petitioner initially reported. However, the leap from this possibility to the conclusion that a suspected vaccine skin reaction (which itself, on this record, is not all that well-established evidentiarily) could initiate a cancerous process thereafter, manifesting as a benign tumorous growth, was not sufficiently explained or established by reference to persuasive scientific and medical evidence. I cannot on this record conclude it "more likely than not" that a skin reaction *could* evolve into this kind of tumor, specific to a muscle type not common to the skin (and not the actual, intended location of a vaccination)—or that the vaccine could explain the total course of events, whether due to needle trauma or the vaccine's intended immune system stimulation. Thus, while the claim was unquestionably reasonably pursued, there is not enough evidence generally or specifically in support of it to find for Petitioner.

CONCLUSION

A Program entitlement award is only appropriate for claims supported by preponderant evidence. Here, Petitioner has not made such as showing. Petitioner is therefore not entitled to compensation.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.[15]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[14] I thus do not give great weight to Dr. Amber's speculation that it *could not* be a coincidence. The Vaccine Act's legal standards require more of an evidentiary showing than a *suspicion* of a causal relationship that itself relies on limited circumstantial evidence not bulwarked with other evidence. Were it otherwise, all post-vaccination injuries would be compensable simply because of their odd timing.

[15] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.